Fried potato consumption is associated with elevated mortality: an 8-year longitudinal cohort study

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Short running head: Potato and mortality

Abbreviations: body mass index: BMI; cardiovascular disease: CVD; Center for Epidemiologic Studies Depression: CES-D; confidence intervals: CIs; food frequency questionnaire: FFQ; hazard ratios: HRs; Physical Activity Scale for the Elderly: PASE.

ABSTRACT

Background: Few studies have assessed the association between potato consumption and mortality.

Objective: We investigated whether potato consumption (including fried and unfried potatoes) is associated with increased premature mortality risk in a North American cohort.

Design: A longitudinal analysis included 4,440 participants aged 45-79 years at baseline with 8-year follow-up from the Osteoarthritis Initiative (OAI) cohort study. Potato consumption (including fried and unfried potatoes) was analyzed through a Block Brief 2000 food frequency, and categorized as ≤ 1 time/month, 2-3 times/ month, 1 time/week, 2 times/week, ≥ 3 times/week. Mortality was ascertained through validated cases of death. To investigate the association between potato consumption and mortality, Cox's regression models were constructed to estimate hazard ratios (HRs) with 95% confidence intervals (CIs), adjusting for potential confounders.

Results: Of the 4,400 participants included, 2,551 (=57.9%) were females with a mean age of 61.3±9.2 years. During the 8-year follow-up, 236 of 4400 participants died. After adjusting for 14 potential baseline confounders, and taking those with the lowest consumption of potatoes as the reference group, participants with the highest consumption of potatoes did not have an increased overall mortality risk (HR=1.11; 95%CI: 0.65, 1.91). However, subgroup analyses indicated that participants consuming fried potatoes 2-3 times/week (HR=1.95; 95%CI: 1.11, 3.41) and ≥3 times/week (HR=2.26; 95%CI: 1.15, 4.47) were at increased mortality risk. The consumption of unfried potatoes was not associated with increased mortality risk.

Conclusion: Frequent consumption of fried potatoes appears to be associated with an increased mortality risk. Additional studies with larger sample size should be performed to confirm if overall potato consumption is associated with higher mortality risk.

INTRODUCTION

White potatoes have been a staple food among many traditional diets of the Western world (1). In recent years, the overall consumption of potatoes has declined in the USA, but processed potato intake (e.g. French fries and chips) has dramatically increased (2). Potatoes are rich in starch and have a high–glycemic index, which has been associated with an increased risk of developing obesity, diabetes and cardiovascular disease (CVD) (3). However, compared with other common carbohydrate sources, potatoes have a low energy density because of their high-water content (4). In addition, potatoes provide other important micronutrients, which are all associated with a decreased risk of morbidity and mortality (5). Therefore, potatoes represent a peculiar food since they contain both macro- and micro-nutrients with possible beneficial and harmful effects on health.

The literature regarding potato consumption and common medical conditions is equivocal. A study including three North American cohorts reported that greater consumption of potatoes (i.e. $\geq$7 servings/week) was associated with a 33% higher risk of diabetes, independent of several potential confounders (6). In this study, even the intake of three servings per week was associated with an increased diabetes risk of 4% for baked, boiled, or mashed potatoes, and 19% for French fries (6). The use of fried potatoes is probably associated with higher risk of diabetes and other comorbidities for several reasons, such as cooking with trans-fats (6). These findings were confirmed in the Nurses' Health Study (7). On the contrary, a study conducted in Sweden among 69,313 men and women failed to find any significant associations between higher potato consumption and the risk of CVD morbidity and mortality during a 13-yearfollow-up (8). A systematic review published in 2016, including five observational studies for a total of 170,413 healthy subjects, did not provide any conclusive evidence to suggest an association between potato intake and the risk of developing obesity,

type 2 diabetes and CVD (9). However, in the same study, the consumption of French fries and fried potatoes was associated with a slightly higher risk of obesity and diabetes (9). Despite these previous studies, to the best of our knowledge, no previous study that has investigated whether potato consumption is associated with premature mortality.

Given that potatoes are widely consumed in North America and Europe, and no data is available regarding the association with mortality, the current study aimed to investigate whether higher consumption of potatoes is associated with increased risk of death in a longitudinal cohort study of men and women participating in the Osteoarthritis Initiative. As a secondary objective, we investigated whether higher consumption of fried and unfried potatoes is associated with a higher mortality risk.

METHODS

Data source and subjects

Data were obtained from the Osteoarthritis Initiative database (10), which is available for public access at http://www.oai.ucsf.edu/. The specific datasets utilized were registered during the baseline and screening evaluations (V00), and mortality data was available until 96 months from baseline (V10). The OAI includes patients at high risk of knee osteoarthritis, who were recruited at four clinical centers in the USA (Baltimore, MD; Pittsburgh, PA; Pawtucket, RI; and Columbus, OH) between February 2004 and May 2006. People were eligible if they: i) had knee osteoarthritis and reported knee pain in a 30-day period in the past 12 months or ii) were at high risk of developing knee OA (e.g. overweight/obese, knee injury/operation, parents/siblings with total knee replacement, frequent knee-bending activities that increase risk, and hand/hip osteoarthritis) (10).

All the participants provided written informed consent. The Osteoarthritis Initiative study protocol was approved by the institutional review board of the Osteoarthritis Initiative Coordinating Center, University of California at San Francisco.

Potato consumption (exposure)

Participants' diet patterns were analyzed using the semi-quantitative Block Brief 2000 food frequency questionnaire (FFQ) at baseline (11, 12). This validated tool, containing a food list of 70 items, was designed to assess the individual's food and beverage consumption over the past year. Frequency of food consumption of the included items was reported at nine levels of intake from "never" to "every day". There were also seven dietary behavior questions on food preparation methods and fat intake, one question on fiber intake, and 13 questions regarding vitamins and minerals.

Potato consumption was assessed through two specific questions. The first question considered the consumption of French fries, fried potatoes or hash browns. The second question considered the consumption of white unfried potatoes, including boiled, baked, mashed and potato salad. Although data regarding sweet potatoes were available, this information was not included due to the different composition between sweet and white potatoes. Potato consumption was categorized into five groups from the nine available categories since too few subjects "never" consumed or consumed potatoes "few times", or "more than 4 times/weekly" during the previous year. Therefore, the five categories were: $\leq$ 1 time/month, 2-3 times/ month, 1 time/week, 2 times/week, $\geq$ 3 times/week.

Outcome

The study's outcome of interest was all-cause mortality. In the Osteoarthritis Initiative, mortality was confirmed and adjudicated by several methods (autopsy report, coroner's report, death certificate medical records, National Death Index, obituary or Social Security Death Index).

Covariates

We identified numerous potential confounders which may influence the relationship between potato consumption and mortality including: body mass index (BMI); weekly alcohol consumption, total energy intake and adherence to a Mediterranean diet (12); physical activity evaluated using the Physical Activity Scale for the Elderly (PASE) (13); depressive symptoms evaluated through the Center for Epidemiologic Studies Depression (CES-D) scale (14); ethnicity; smoking habits, educational level and yearly income (< or $\geq$ $50,000 or missing data); and variables pertaining to physical health status. Validated general health measures of self-reported comorbidities were assessed using the modified Charlson comorbidity score

(15). The medical morbidities that were assessed using this score included diseases/disorders that were common in North Americans such as fractures, heart attack and failure, stroke, diabetes and cancer (16).

Statistical analyses

Normal distributions of continuous variables were tested using the Kolmogorov-Smirnov test. Data are shown as means±standard deviations (SDs) for quantitative measures, and frequency and percentages for all discrete variables. P values for trends were calculated using the Jonckheere-Terpstra test for continuous variables and the Mantel-Haenszel Chi-square test for categorical variables.

Incidence rates are reported as number of deaths for 1,000 persons-years. The proportional hazards assumption was checked by plotting the Schoenfeld residuals versus time without any violation and then Cox's regression analyses were performed (18). The basic model was adjusted for age and sex. In addition to age and sex, the fully adjusted model adjusted for: ethnicity (whites vs. others); BMI (as continuous); education (degree vs. others); smoking habits (current and previous vs. others); yearly income (categorized as $\geq$ or < 50,000$, missing data); PASE (as continuous); Charlson co-morbidity index (as continuous); daily energy intake (as continuous); CES-D scale (as continuous). These covariates used for adjustment were factors significantly different across potato consumption categories (considering a p-value<0.10) or significantly associated with death according to univariate analysis (p-value<0.05). We also ran the same analyses and investigated the association between consumption of fried and unfried potatoes and mortality separately. In these analyses, we added the consumption of unfried potatoes in the model when conducting the

analyses for fried potatoes and vice versa. In all the analyses, Cox's regression analysis data are reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

To test the robustness of our analyses, sensitivity analyses were conducted evaluating the interaction between potato consumption and selected factors (e.g. sex, race, education, smoking habits, yearly income and presence/absence of diseases at baseline, BMI above or below 25 Kg/m^2) in predicting mortality, but no moderator emerged as significant. Multi-collinearity among covariates was assessed using the variance inflation factor, with a score of 2 leading to the exclusion of a variable, but no parameter was excluded for this reason.

All the analyses were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, Illinois). All statistical tests were two-tailed and statistical significance was assumed for a p-value <0.05.

RESULTS

Sample selection

The Osteoarthritis Initiative dataset initially included a total of 4,796 North American participants. At baseline, 130 subjects were excluded due to insufficient information on potato consumption and another 266 had implausible calorie intake (less than 800 and greater than 4,200 Kcal for men; less than 500 and greater than 3,500 Kcal for women). Thus, 4,400 participants were eligible for this study (**Supplemental Figure 1**).

Descriptive characteristics

Of the 4,400 participants, 2,551 were females and 1,849 males. Mean age was 61.3 years (±9.2 years; range: 45-79). Most subjects consumed potatoes (n=1,174; 26.7%) 2-3 times during a month.

Table 1 shows the participants' characteristics by total potato intake. Those consuming potatoes $\geq$ 3 times/week (reflecting the highest consumption of potatoes) were older (p for trend<0.0001), more likely to be male (p for trend<0.0001), white (p for trend<0.0001), with a lower educational level (p for trend<0.0001) with respect to those in the other categories. They were also less adherent to a Mediterranean diet (p for trend <0.0001) and had more co-morbidities (p for trend=0.003) than other participants, in particular CVDs (**Table 1**).

Potato consumption and mortality

During the 8-year follow-up, 236 people (=5.4% of the baseline population) died, indicating a global mortality rate of 13 (95%CI: 11-17)/1,000 persons-years.

Table 2 illustrates the association between overall potato consumption and mortality. The non-adjusted incidence of mortality was three times as high in those consuming the highest amount of potatoes ($\geq$ 3 times/week) compared to those consuming potatoes less than 1 time/month. However, using a Cox's regression analysis, adjusted for 14 potential baseline confounders, and taking those with the lowest consumption of potatoes as the reference, the participants with the highest consumption of potatoes did not have any increased risk of mortality (HR=1.11; 95%CI: 0.65, 1.91; p=0.71; **Table 2**).

Table 3 shows Cox's regression analyses for fried and unfried potatoes taking death as the outcome. After adjusting for all baseline potential confounders, higher consumption of unfried potatoes was not associated with any increased risk of death (HR=0.89; 95%CI: 0.51, 1.55; p=0.67 for participants consuming non-fried potatoes $\geq$ 3 times/week vs. $\leq$1 time/month). On the contrary, the relative risk of mortality was more than doubled among those who consumed fried potatoes more than twice a week (HR=1.95; 95%CI: 1.11, 3.41; p=0.02) or $\geq$ 3 times a week (HR=2.26; 95%CI: 1.15, 4.47; p=0.02).

DISCUSSION

In this cohort study, we found that overall white potato consumption was not associated with a higher risk of mortality, after adjusting for pertinent confounders. However, consuming fried potatoes more than twice a week was consistently associated with an increased mortality risk in this population of older adults.

Overall, in this cohort the consumption of potatoes was very high. The great majority of the participants included in the OAI, in fact, consumed potatoes at least 2 or 3 times per month, and a third of them 3 or more times per week. This intake is in line with the data of a 2013 report of the US Department of the Agriculture showing that on average American citizens consumed 115.6 pounds of white potatoes per year, of which, about two thirds are French fries, potato chips and other frozen or processed potato products (2). White potatoes accounted for 30% of the 384.4 pounds per person of vegetables and legumes intake (2). In our cohort, higher intake of potatoes was associated with several other potential mortality risk factors, such as male sex (19), higher frequency of co-morbidities, higher BMI (20), and lower adherence to a Mediterranean diet score. However, to our knowledge it has not been established whether frequent potato consumption is associated with higher mortality risk, independently of adiposity and other age-associated metabolic conditions/diseases.

In our study, overall potato consumption was not associated with an increased risk of all-cause mortality, in partial agreement with other published data (8). The only study addressing mortality, in fact, was limited by the fact that only CVD mortality was considered and did not find any association between higher consumption of potatoes and CVD-related death risk (8). It is possible that the high content of fiber, vitamins and micronutrients in white potato could have counterbalanced the detrimental effects of their high glycemic index (5). However, given

that this is an emerging field and that our data are preliminary, larger prospective studies are required to further investigate this relationship.

Despite overall potato consumption was not related with mortality, interestingly, our data suggest that the consumption of fried potatoes is associated with a significant higher risk of mortality. Consuming fried potatoes more than twice a week was associated with a more than doubled risk of death independently of several other confounders. Many factors could explain these findings. First, French fries and fried potatoes typically contain high levels of dietary fat (including trans-fat) and added salt, which may increase the risk of death, particularly for CVD (21). Second, a higher consumption of fried potatoes could increase the risk of other chronic diseases, such as obesity (22, 23), hypertension (24) and diabetes (6), which are also powerful risk factors for CVD. One epidemiological study conducted in Sweden found no association between fried potatoes intake and CVD mortality (8). Therefore, more studies are warranted to understand whether higher fried potatoes consumption is associated with higher CVD and cancer mortality, due to higher intake of trans fatty acids, oxidized lipids, acrolein, acrylamide, furan, and glycidamide (25, 26). Third, people consuming fried potatoes more frequently might have other unhealthy dietary habits, such as increased consumption of processed red meat, salty foods and sugar-sweetened beverages, which may increase *per se* the risk of death (27, 28). Finally, a lower socio-economic status could play a role in the association between high fried potatoes consumption and mortality. However, in our study this association was still significant even after we adjusted our analyses for both education and income levels, suggesting a marginal role of the socio-economic status.

Whilst our data are relatively novel, some limitations should be noted. The main limitation is that we were not able to assess cause-specific mortality. Second, we were unable to assess the influence of bio-humoral markers (e.g. inflammation, insulin-resistance, oxidative stress) on

the association between potato consumption and mortality. Third, the medical conditions were self-reported and could have introduced some level of bias. Fourth, nutritional intake could have suffered from selective and potentially inaccurate recall and this may have influenced our results. Finally, as we did not consider changes in dietary habits between baseline and the follow-up, this too could have introduced bias.

In conclusion, our data suggest that overall potato consumption was not associated with higher risk of death in a cohort of North American people. On the contrary, frequent consumption of fried potatoes significantly increased overall mortality risk. Future studies are warranted to elucidate the role of potato consumption on cause-specific mortality.

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Authors' contribution: NV, MN and AK analyzed the data; BS, MS, AV, JD, DN wrote the paper; GC, PS, SM, LF gave a critical revision of the final version; NV had primary responsibility for final content. All authors read and approved the final manuscript.

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Table 1. Characteristics of the participants classified according to their frequency of potato consumption.

	≤ 1 time/month (n=761)	2-3 times/ month (n=1174)	1 time/week (n=930)	2 times/week (n=942)	≥ 3 times/week (n=593)	P value for trend[1]
General characteristics						
Age (years)	61.4 (8.7)	60.9 (9.2)	61.0 (9.0)	60.9 (9.4)	63.1 (9.6)	<0.0001
PASE (points)	157.4 (79.7)	162.0 (83.6)	165.1 (80.0)	163.5 (83.5)	150.5 (80.6)	0.006
Females (n, %)	530 (69.6)	699 (59.5)	514 (55.3)	493 (52.3)	315 (53.1)	<0.0001
White race (n, %)	593 (78.0)	890 (75.9)	776 (83.4)	780 (82.9)	485 (81.8)	<0.0001
Smoking (previous/current) (n, %)	371 (49.1)	557 (47.6)	425 (46.0)	430 (45.8)	295 (49.9)	0.77
Graduate degree (n, %)	269 (35.4)	346 (29.5)	292 (31.4)	274 (29.1)	147 (24.8)	<0.0001
Yearly income (≥ $50,000)	451 (59.3)	677 (57.7)	617 (66.3)	555 (58.9)	293 (49.4)	0.03
Nutritional parameters						
Energy intake (Kcal/day)	1149.7 (424.7)	1308.7 (474.1)	1435.5 (484.6)	1600.5 (564.9)	1745.4 (644.9)	<0.0001
Alcohol drinks (in a week)	1.75 (1.46)	1.73 (1.46)	1.77 (1.44)	1.74 (1.54)	1.71 (1.56)	0.94
Adherence to Mediterranean diet (points)	27.6 (5.6)	27.4 (4.9)	27.8 (4.7)	28.6 (4.7)	30.0 (5.3)	<0.0001
Medical conditions						
BMI (Kg/m^2)	28.0 (4.7)	28.8 (4.8)	28.9 (4.8)	28.9 (4.8)	28.5 (4.8)	0.001

	≤ 1 time/month (n=761)	2-3 times/ month (n=1174)	1 time/week (n=930)	2 times/week (n=942)	≥ 3 times/week (n=593)	P value for trend[1]
CES-D (points)	6.5 (7.3)	6.7 (7.1)	6.3 (6.3)	6.5 (6.9)	7.2 (7.3)	0.18
Charlson co-morbidity index (points)	0.4 (1.0)	0.4 (0.8)	0.3 (0.8)	0.4 (0.8)	0.5 (1.0)	0.003
Fractures (n, %)	135 (17.8)	200 (17.1)	161 (17.4)	158 (16.8)	130 (22.0)	0.14
Heart attack (n, %)	8 (1.1)	27 (2.4)	13 (1.4)	17 (1.8)	22 (3.7)	0.02
Heart failure (n, %)	12 (1.6)	21 (1.8)	15 (1.6)	22 (2.4)	18 (3.1)	0.04
Stroke (n, %)	21 (2.8)	41 (3.5)	24 (2.6)	29 (3.1)	18 (3.1)	0.96
Diabetes (n, %)	62 (8.3)	97 (8.4)	64 (7.0)	66 (7.2)	52 (8.9)	0.78
Cancer (n, %)	37 (4.9)	65 (5.5)	40 (4.3)	38 (4.0)	32 (5.4)	0.59

Notes: The data are presented as means (with standard deviations) for continuous variables and number (with percentage).

[1] P values for trends were calculated using the Jonckheere-Terpstra test for continuous variables and the Mantel-Haenszel Chi-square test for categorical varaibles.

Abbreviations: BMI: body mass index; CES-D: Center for Epidemiologic Studies Depression; PASE: Physical Activity Scale for the Elderly.

Table 2. Association between potato consumption and mortality.

	Incidence (95% CI)	Basic-adjusted [1] HR (95%CI)	P value	Fully-adjusted[2] HR (95%CI)	P value
≤ 1 time/month	6 (3-10)	1 [reference]		1 [reference]	
2-3 times/ month	12 (4-19)	1.04 (0.65, 1.64)	0.89	1.16 (0.72, 1.87)	0.54
1 time/week	10 (6-14)	1.21 (0.76, 1.40)	0.43	1.34 (0.82, 2.18)	0.24
2 times/week	16 (9-22)	1.36 (0.86, 2.15)	0.18	1.59 (0.98, 2.57)	0.06
≥ 3 times/week	18 (7-29)	0.94 (0.56, 1.56)	0.80	1.11 (0.65, 1.91)	0.71

Notes:

[1] Basic-adjusted model included as covariates age (as continuous) and sex.

[2]Fully-adjusted model included as covariates: age (as continuous); sex; race (whites vs. others); body mass index (as continuous); education (degree vs. others); smoking habits (current and previous vs. others); yearly income (categorized as ≥ or < 50,000$ and missing data); Physical Activity Scale for Elderly score (as continuous); Charlson co-morbidity index (as continuous); daily energy intake (as continuous); alcoholic drinking (during a week); adherence to Mediterranean diet score; Center for Epidemiologic Studies Depression scale (as continuous).

Abbreviations: CI: confidence intervals; HR: hazard ratio.

Table 3. Association between fried and not fried potato consumption and mortality.

	Incidence (95% CI)	Basic-adjusted [1] HR (95%CI)	P value	Fully-adjusted [2] HR (95%CI)	P value
Unfried potatoes					
≤ 1 time/month	9 (2-17)	1 [reference]		1 [reference]	
2-3 times/ month	12 (6-17)	1.15 (0.75, 1.75)	0.53	1.24 (0.81, 1.91)	0.33
1 time/week	13 (5-20)	1.16 (0.74, 1.82)	0.53	1.18 (0.73, 1.90)	0.50
2 times/week	21 (10-33)	1.44 (0.94, 2.20)	0.09	1.50 (0.94, 2.39)	0.09
≥ 3 times/week	12 (4-19)	0.82 (0.49, 1.37)	0.44	0.89 (0.51, 1.55)	0.67
Fried potatoes					
≤ 1 time/month	10 (6-14)	1 [reference]		1 [reference]	
2-3 times/ month	12 (7-18)	1.38 (0.98, 1.90)	0.07	1.37 (0.99, 1.91)	0.06
1 time/week	9 (5-13)	1.12 (0.73, 1.72)	0.61	1.10 (0.70, 1.71)	0.68
2 times/week	18 (6-31)	1.90 (1.10, 3.27)	0.02	1.95 (1.11, 3.41)	0.02
≥ 3 times/week	32 (7-57)	2.56 (1.35, 4.83)	0.004	2.26 (1.15, 4.47)	0.02

Notes:

[1]Basic-adjusted model included as covariates age (as continuous) and sex.

[2] Fully-adjusted model included as covariates: age (as continuous); sex; race (whites vs. others); body mass index (as continuous); education (degree vs. others); smoking habits (current and previous vs. others); yearly income (categorized as missing, ≥ or < 50,000$ and missing data); Physical Activity Scale for Elderly score (as continuous); Charlson co-morbidity index (as continuous); daily energy intake (as continuous); alcoholic drinking (during a week); adherence to Mediterranean diet score; Center for Epidemiologic Studies Depression scale (as continuous).

In the elaborations regarding unfried potatoes, the consumption of fried potatoes was added as covariate in the fully-adjusted model and vice versa.

Abbreviations: CI: confidence intervals; HR: hazard ratio.